REMARKS

STATUS OF THE CLAIMS

Claims 66-71 and 125-128 are pending as shown in the Response mailed December 8, 2004.

INVENTORSHIP/DECLARATION

Applicants note with appreciation that inventorship has been changed to reflect that Alan WOLFFE and Fyodor URNOV are the inventors of the pending claims. Applicants also note that the revised declaration including the name, address and citizenship of Alan Wolffe's legal representative Elizabeth Wolffe has been accepted.

OBJECTIONS/REJECTIONS WITHDRAWN

Applicants note that their amendments have resulted in withdrawal of all the previous objections to the specification. In addition, Applicants note that the rejections of claims 1-6, 8-15, 21-26 and16-20 under 35 U.S.C. § 112, first paragraph, enablement; claims 66-71 under 35 U.S.C. § 112, second paragraph; and claims 1-26 under 35 U.S.C. § 103(a) in view of various references have been withdrawn. Withdrawal of the obviousness-type double patenting rejection of claims 1-26 is also noted.

CLAIMED SUBJECT MATTER

Applicants wish to point out that presently-pending claims 66 and 125-128 recite a polynucleotide (not a library) that is obtained as a result of following a specifically recited process. Applicants respectfully urge the Office to consider the claimed subject matter in its determination of novelty and of compliance with 35 U.S.C. § 112.

35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 66-71 and 125-128 are rejected under 35 U.S.C. § 112, first paragraph as allegedly not described by the specification as filed. (Office Action, paragraph 16). As previously, it is maintained that the written description requirement is not satisfied because an insufficient number of representative species of the claimed genus are disclosed. *Eli Lilly* is again cited in support of the rejection. Furthermore, Applicants previous arguments were deemed unpersuasive on the grounds that no "evidence or arguments [were provided] as to how the specification of the instant application conveys with reasonable clarify to those skilled in the art, as of the filing date sought, that applicants were in possession of the invention as now claimed." (Office Action, page 7).

Applicants again traverse the rejection and supporting remarks.

For the reasons of record, which Applicants note were not addressed in the Final Office Action, the Office's reliance of *Regents of the Univ. Calif. v. Eli Lilly* remains misplaced. The written description requirement of § 112 is highly fact-dependent and the claims, disclosure and state of the art in *Eli Lilly* are entirely different from those in the case at hand. Indeed, the issue in *Eli Lilly* was whether a human insulin cDNA was patentable before it had been isolated and characterized. The application in that case had not described either the isolation or the sequence of human insulin cDNA. By contrast, in the present application, isolation of the claimed libraries (claims 67-71) has been described (*see, e.g.*, Example 15, pp. 123-126 of the specification, noting it is an actual, not a prophetic, example); moreover, the polynucleotides recited in claims 116 and 125-128 have been obtained and representative sequences have been determined and described (*see, e.g.*, SEQ ID NOS. 10, 11 and 12). Thus, not only is the Federal Circuit's holding *Eli Lilly* irrelevant to the question of whether the written description requirement is fulfilled for the presently-claimed subject matter; in addition, Applicants have made the skilled artisan aware of their possession of the claimed subject matter, as required to satisfy the first paragraph of Section 112.

It is also noteworthy that the Court in *Eli Lilly* quoted *Fiers v. Revel* to the effect:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name, or physical properties, as we have held, then a description also requires that degree of specificity. (*Lilly* at 1240, emphasis added)

In this light, Applicants point out that the claimed subject matter in the present application is not a single sequence encoding a known protein, as it was in *Lilly*; rather the pending claims recites libraries of polynucleotides and individual polynucleotide members of the claimed libraries. By its very nature, a library contains a number of different sequences, and it is impossible to predict the identity of the sequences that will be obtained after construction of a library. Thus, conception of the claimed libraries does not, indeed it cannot, require description of the nucleotide sequence of every member of the library. Despite the inability to predict the nucleotide sequence of each and every member of the claimed libraries, one of skill in the art would be aware Applicants were in possession of methods for making libraries of accessible regions of cellular chromatin, and of the libraries obtained through the practice of those methods. The skilled artisan, having followed the teaching of the specification, would have no doubt that s/he was in possession of a sequence corresponding to an accessible region of cellular chromatin, or to a library of such sequences.

Applicants also note that because the claims at issue are product-by-process claims, the proper standard for determining whether the written description requirement is as set forth in M.P.E.P. § 2163, which states that "where the process has actually been used to produce the product, the written description requirement for a product-by-process claim is clearly satisfied." Applying this clearly stated standard with respect product by process claims, it is clear that the specification as filed more than adequately describes the claimed libraries (as made by the claimed method steps). The process as set forth in the claims has actually been used to produce libraries. Thus, the rejection of the pending product by process claims may be properly withdrawn.

Finally, as noted above, claims 116 and 125-128 recite polynucleotides, for which representative examples have been provided. Additional examples of polynucleotide sequences that have been obtained according to the claims would do nothing to further describe the invention and are therefore unnecessary.

For all of the foregoing reasons, the rejection for lack of written description is improper and should be withdrawn.

35 U.S.C. § 102(B)

Claims 66-71 and 125-128 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by the Clontech Catalogue. (Office Action, paragraph 17). In support of this rejection and in response to Applicants' previous arguments, the Examiner makes the following assertions:

1. "the insert of each clone in the claimed library . . . comprise[s] polynucleotides that correspond to the accessible region and inaccessible regions of the cellular chromatin." (*Final Office Action* at page 10)

2. the libraries disclosed by the reference ". . . inherently have clones with inserts that are only from the accessible region, and clones with an insert that comprises polynucleotide from the accessible region and the inaccessible region." (*Final Office Action* at pages 10-11)

Both of the foregoing statements are unsupported assertions and the first is flatly untrue. First, polynucleotides that correspond to inaccessible regions of cellular chromatin are not covered by the pending claims. Second, the steps used to the make the claimed polynucleotides and claimed libraries insure that accessible regions of cellular chromatin are cloned. The Examiner has provided absolutely no evidence that indicates otherwise.

With respect to the second assertion, Applicants traverse the unsupported assumption that Clontech's libraries inherently "consist essentially of" accessible regions. First of all, the

Examiner has provided no evidence that even a single clone in the Clontech library contains only sequences corresponding to an accessible region of cellular chromatin. Furthermore, it is axiomatic that in order to support an anticipation rejection based on inherency, the Office must provide factual and technical grounds establishing that the inherent feature necessarily and inevitably flows from the teachings of the reference. *See, e.g., Ex parte Levy*, 17 USPQ2d 1461, 1464 (BPAI 1990). Inherency cannot be established by probabilities or possibilities. *See, e.g., Continental Can Co. USA, Inc. v. Monsanto Co.* 20 USPQ2d 1746, 1749 (Fed. Cir. 1987).

In the pending case, as previously noted, digestion of naked DNA (as described in Clontech) will necessarily result in a collection (library) of DNA fragments that include both accessible and nonaccessible regions, as there are no proteins in naked DNA to protect the sequences from digestion. In stark contrast, the claimed libraries include only fragments including accessible regions,[1] as they are made from digestion of cellular chromatin. In other words, contrary to the Office's assertion, libraries produced by Clontech's methods will inherently produce libraries including fragments from non-accessible regions. Such fragments are not encompassed by the pending claims. Simply put, because a library consisting essentially of accessible regions is **not** an inherent feature of Clontech's libraries, the Clontech catalog does not anticipate the pending claims.

Furthermore, the process steps recited in the pending claims impart structural and functional differences of the claimed libraries as compared to the libraries described in the Clontech catalog. Digestion of naked DNA (Clontech) will necessarily give any number of fragments that may or may not correspond to accessible regions, while digestion of cellular chromatin (as claimed), with its associated proteins, protect non-accessible regions and result in a library that does not contain fragments representing non-accessible regions. Thus, Clontech fails to describe, expressly or inherently, polynucleotides and libraries as claimed. Therefore, the rejection cannot be sustained and Applicants respectfully request withdrawal thereof.

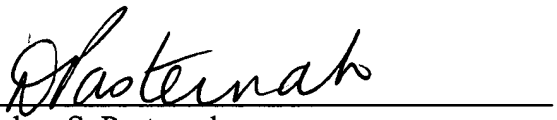
[1] Despite the Examiner's unsupported assertion to the contrary

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

Respectfully submitted,

Date: May 24, 2005

By: 

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